11:45

**INHIBITION OF L-ARGININE METABOLISM RESULTS IN GREATER ATTENUATION OF ENDOTHELIUM-DEPENDENT RESPONSES TO ACETYLCHOLINE IN THE SPONTANEOUSLY HYPERTENSIVE STROKE-PRONE RAT (SHRSP).**

Linda Lee, R. Clinton Webb, University of Michigan, Ann Arbor, MI

Nitric oxide (NO) is a major endothelium-derived vascular smooth muscle relaxing factor (EDRF). L-Arginine (L-Arg) the proposed physiologic precursor for NO is specifically inhibited by L-Arg analog $N^G$-monomethyl-L-Arginine (L-NMMA). The goal of this experiment was to assess arginine metabolism as a factor in enhanced constrictor activity in aortic rings of SHRSP. Relaxation responses to the cumulative addition of Ach ($10^{-10}$-$10^{-4}$M) in SHRSP(n=6) aortic rings did not differ from those in WKY(n=6, ED50=$10^{-8}$M). Incubation with L-NMMA (30$\mu$M) caused complete inhibition of the relaxation responses to Ach in SHRSP, whereas in the WKY the magnitude of inhibition was only 50%. L-Arg(10-100$\mu$M) reversed the inhibitory effect of L-NMMA on Ach-induced relaxation in both SHRSP and WKY. Relaxation responses to cumulative addition of A23187 ($10^{-10}$- 3x$10^{-10}$M) in SHRSP (n=6) aortic rings did not differ from those in WKY (n=5). Incubation with L-NMMA (30$\mu$M) caused complete inhibition of relaxation to A23187 in both SHRSP and WKY. L-ARG (10-100$\mu$M) reversed the inhibitory effect of L-NMMA. These data support the hypotheses that the production of NO in SHRSP is augmented as compared to normotensive WKY rats and that this increased production of NO masks increased smooth muscle contraction to acetylcholine. Since ACH initiates its endothelial action by muscarinic receptor-mediated activation of phoshcolipase C, these results also indicate that SHRSP endothelial cells may have an abnormal phosphoinositide signal that contributes to the production of a vasoactive substances.

## Wednesday, March 6, 1991
## 10:30AM–12:00NOON, Room 254, West Concourse
## Detection and Analysis of Intravascular Plaque and Thrombus

10:30

**DOES CORONARY ANGIOGRAPHIC MORPHOLOGY INDICATE PLAQUE CONTENT?**

Uri Rosenschein, Ronald J.L. Dick, Christian C. Haudenschild, Eric J. Topol, M.D., University of Michigan, Ann Arbor, MI

The pre-angioplaty assessment of pts angiography is currently used to assess the procedural outcome using the ACC/AHA criteria. We hypothesized that actual lesion composition may coincide with the prospective angiographic assessment. To test the hypothesis, we assessed the pre-atherectomy angiograms of 57 pts and classified the lesions according to the ACC/AHA criteria and compared this to the excised lesion's light microscopic features as assessed by morphometric analysis: fibrocellular (F/C), sclerotic (Scl), atheromatous (Ath), organizing thrombus (O/Th) and fresh thrombus (F/Th).

| Class | F/C (%) | Scl (%) | Ath (%) | O/Th (%) | F/Th (%) |
|---|---|---|---|---|---|
| Type A (n=12) | 40±28 | 40±20 | 13±15 | 6±7 | 1±2 |
| Type B (n=35) | 31±24 | 44±30 | 9±10 | 7±18 | 9±19 |
| Type C (n=10) | 31±25 | 39±20 | 16±23 | 10±19 | 4±9 |
| p value | NS | NS | NS | NS | NS |

The ACC/AHA criteria assesses both lesion morphologic features of lesion complexity (e.g. thrombus, irregularity) and also the position of the lesion (e.g. bifurcation, ostial). To eliminate the influence of the locational features, the morphologic features of lesion complexity were compared to the histology. There was no difference noted when lesions with no complex features, one complex feature and greater than one feature were compared to the plaque composition. Conclusions: (1) Atherosclerotic plaque content in all groups is made up primarily of fibrocellular and sclerotic tissue; (2) Angiographic features do not predict plaque histology; (3) The similarities of plaque composition suggests that that ACC/AHA risk stratification may be more influenced by the position of the lesion rather than the lesion morphology.

10:45

MORPHOLOGIC-ANGIOGRAPHIC CORRELATION AT THE SITE OF PTCA

Takahiko Naruko, Makiko Ueda, Hideki Wanibuchi, Osamu Tojo
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Morphologic-angiographic correlation at the site of PTCA has not been fully clarified. In this study, we examined various angiographic patterns visualized at the site of PTCA and correlated these patterns with morphologic changes induced by PTCA. Sixteen PTCA sites from necropsy patients who had undergone elective PTCA were available for analysis. Angiographic patterns of the PTCA sites were classified into smooth walled dilation, coronary dissection, intraluminal haziness, marginal irregularity, and filling defect due to thrombus. Morphologic dilation injury patterns were divided into three groups: intimal injury only, laceration extending into the media (intimal-medial injury), and no evidence of injury.

| Angiographic appearance at PTCA site | Morphologic findings at PTCA site: No | Intimal injury only | Intimal-medial injury | No injury |
|---|---|---|---|---|
| Smooth-walled | 8 | 2 | 6 | 0 |
| Dissection | 5 | 0 | 5 | 0 |
| Haziness | 3 | 0 | 3 | 0 |
| Irregularity | 0 | 0 | 0 | 0 |
| Thrombus | 0 | 0 | 0 | 0 |
| Totals | 16 | 2 | 14 | 0 |

Conclusion
These findings suggest that angiographic patterns of dissection and haziness visualized at the site of PTCA are closely related to morphologic changes of arterial wall laceration extending into the media.

11:00

**IN VIVO SPECTROSCOPY OF HUMAN CORONARY STENOSES**

Philippe Douek, Antonio Bartorelli, Gad Keren, Moshe Flugelmann, Rosaly Correa, Robert F. Bonner, Martin B. Leon, NIH, Bethesda, MD

Perforations and appropriate laser dosimetry remain problems in laser coronary angioplasty (LCA). Fluorescence identification of target composition and catheter tissue contact has been proposed to provide real-time feedback during LCA. UV-laser excited fluorescence spectra (375-640nm) of coronary obstructions (mean stenosis: 97±3%) were obtained in vivo during LCA in 10 patients and from 30 coronary atherectomy specimens from 10 patients. Analysis of 243 in vivo spectra and correlation with histology of 350 atherectomy spectra were performed using a variety of new algorithms including a ratio test unaffected by thin layers of blood.
**RESULTS:** Spectra and histology of atherectomy specimens manifested high intra- and inter-patient variability demonstrating either fibrous plaque with dense collagen matrix (n=11), smooth muscle cells (SMC) (n=5), mixed collagen matrix and SMC (n=12), or thrombus (n=2), but the spectra were predictive of histology in 28 of the 30 specimens. In 2 patients with restenosis, fluorescence spectra indicated a high concentration of proliferative cells (confirmed by histology) which gave fluorescence spectra indistinguishable from normal media. In clinical trials of LCA, we observed spectra indicative of 1) strong absorption by thin layers of blood between the multifiber catheter and the lesion which altered both laser dosimetry and fluorescence spectroscopy and 2) a heterogeneity in composition of both high grade stenoses and occlusions. The spectral ratio test indicated that 1) all six restenosis lesions contained regions of predominantly smooth muscle cell proliferation and 2)76%±22% of the fibers were directed at blood layers>30µm during laser sequences.
**CONCLUSION:** Fluorescence spectroscopy allows identification of target composition and catheter contact which are critical for reliable dosimetry during LCA; but the histological variability of coronary lesions may limit fluorescence guidance, particularly in restenoses whose spectra can be indistiguishable from normal vessel wall.